

## **REMARKS**

By this amendment, pending claims 1, 18 and 19 have been amended. Support for the amended claims is found in the originally filed claims and in the present specification. For example, see page 6, lines 2-20; page 7, lines 21-27 and page 10, line 29 through page 12, line 9, of the present specification. Accordingly, no new matter has been added by the amendments to the claims. The claims were also amended to correct the spelling of deoxyribonucleotide in several instances.

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, a Sequence Listing in paper and in electronic forms (CRF) has been provided. The required Statement Accompanying Sequence Listing is also included. Applicants respectfully request that this Sequence Listing be entered into the application.

## **Summary of the Office Action**

1. Claims 1-19 were rejected under 35 U.S.C. 112 (second paragraph) as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.
2. Claims 1-19 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent 5,849,902.

## **Response to the Office Action**

Claims 1-19 were rejected under 35 U.S.C. 112 (second paragraph) as being indefinite for use of the term "capable of" in claims 1, 18 and 19. Claims 1, 18 and 19 have been amended to substitute the term "which hybridizes" for the rejected claim language. Thus, amended claims 1, 18 and 19, as well as dependent claims 2-17, do not contain any of the language rejected by the Office Action and Applicants respectfully request that the rejection under 35 U.S.C. 112 (second paragraph) be withdrawn.

Claims 1-19 were rejected by the examiner under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent 5,849,902. In response to the rejection, Applicants submit the attached terminal disclaimers under 37 C.F.R. 1.321(c) executed on behalf of the assignees, Oligos Etc. and Tod M. Woolf. A certificate under 37 C.F.R. 3.73(b) executed on behalf of Oligos Etc. is also submitted herewith. The terminal disclaimers disclaim any right to patent term beyond that of U.S. Patent 5,849,902. In view of the terminal disclaimers, Applicants respectfully

request that the rejection based on the judicially created doctrine of obviousness-type double patenting be withdrawn.

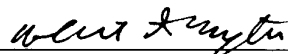
**Conclusion**

Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned Version with markings to show changes made.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: **August 30, 2001**  
Morgan, Lewis & Bockius LLP  
Customer No. **09629**  
1111 Pennsylvania Ave., NW  
Washington, D.C. 20004  
202-739-3000

Respectfully submitted  
**Morgan, Lewis & Bockius LLP**

  
\_\_\_\_\_  
Robert Smyth  
Registration No. 50,801

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**Claim 1 has been amended as follows:**

1. (Once Amended) A chimeric antisense oligonucleotide comprising: a 5' terminus; a 3' terminus and from 11 to 59 5' → 3'-linked nucleotides ~~[capable of]~~ which contiguously ~~[hybridizing]~~ hybridize to a specific RNA and which are independently selected from the group consisting of 2'-modified phosphodiester nucleotides, and 2'-modified P-alkyloxyphosphotriester nucleotides; and wherein said 11 to 59 5' → 3'-linked nucleotides are divided by an RNase H-activating region ~~[capable of]~~ which contiguously ~~[hybridizing]~~ hybridizes to the specific RNA and comprises ~~[of]~~ between three and ten contiguous phosphorothioate-linked deoxyribonucleotides, and wherein the 3' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester nucleotide, and wherein the 5' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester nucleotide.

**Claim 18 has been amended as follows:**

18. (Once Amended) A method of specifically cleaving an RNA in a cell containing RNase H which comprises administering an effective amount of an oligonucleotide complementary to the RNA comprising: a 5' terminus; a 3' terminus; and from 11 to 59 5' → 3'-linked nucleotides ~~[capable of]~~ which contiguously ~~[hybridizing]~~ hybridize to the RNA and which are independently selected from the group consisting of 2'-modified phosphodiester nucleotides, 2'-modified P-alkyloxyphosphotriester nucleotides; and wherein said 11 to 59 5' → 3'-linked nucleotides are divided by an RNase H-activating region ~~[capable of]~~ which contiguously ~~[hybridizing]~~ hybridizes to the RNA and comprises ~~[of]~~ between three and ten contiguous phosphorothioate-linked deoxyribonucleotides, and wherein the 3' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate ~~[deoxyribonucleotides]~~ deoxyribonucleotides, phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester-linked nucleotide, and wherein the 5' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate

[~~deoxyribonucleotides~~] deoxyribonucleotides, phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester-linked nucleotide.

**Claim 19 has been amended as follows:**

19. (Once Amended) A chimeric antisense oligonucleotide comprising:

- a) an RNase H activation region [~~capable of~~] which contiguously [~~hybridizing~~] hybridizes to a specific RNA and which has between 5 and 10 contiguous deoxyphosphorothioate nucleotides;
- b) between 4 to 59 contiguous 5' → 3'-linked 2'-methoxyribonucleotides [~~capable of~~] which contiguously [~~hybridizing~~] hybridize to the specific RNA; and
- c) an exonuclease blocking group present at the 3' end, the 5' end, or both the 3' and 5' ends of the oligonucleotide drawn from the group consisting of: a non-5' → 3' phosphodiester-linked nucleotide, from one to three contiguous 5' → 3'-linked modified nucleotides, and a non-nucleotide chemical blocking group.



RECEIVED  
PATENT

Attorney Docketed ~~054800-5008-01~~

TECH CENTER 1600 2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Amy Arrow *et al.*** )  
 )  
Application No. **09/211,794** ) Group Art Unit: **1635**  
 )  
Filed: **December 15, 1998** ) Filed: **Mary Schmidt**  
 )  
For: **Three Component Chimeric Antisense** )  
**Oligonucleotides** )

**CERTIFICATE UNDER 37 C.F.R. 3.73(b)**

Oligos Etc. Inc., a corporation of the state of Oregon, located at 9775 S.W. Commerce Circle, Wilsonville, Oregon 97070, certifies that it is the assignee of less than the entire right, title and interest in the patent application identified above. The extent of its ownership interest, by percentage, is fifty (50) by virtue of a chain of title from the inventors, of the patent application identified above, to the current assignee as shown below:

1. From: **Amy ARROW, Roderic M. K. DALE and Tod M. WOOLF**

To: **Oligo Therapeutics Inc. Oligos Etc. Inc. and Tod M. Woolf**

The document was recorded in the U.S. Patent and Trademark Office on December 17, 1999 at

Reel **010464**, Frame **0576**.

2. From: **Oligo Therapeutics Inc.**

To: **Oligos Etc. Inc.**

The document was recorded in the U.S. Patent and Trademark Office on December 29, 1999 at

Reel **010504**, Frame **0349**.

The undersigned has reviewed all the documents in the chain of title of the patent identified above and, to the best of undersigned's knowledge and belief, title is in the assignee identified above. The undersigned (whose title is supplied below) is empowered to act on behalf of the assignee.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or

imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

**Oligos Etc. Inc.**

Name: **Roderic M. K. Dale**  
Title: **President and C.E.O.**

Signature: 